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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,914	09/15/2003	Xingen Lei	19603/4261 (CRF D-2895A)	2510

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EXAMINER
MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,914	LEI ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-34,38 and 43-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-34,38 and 43-53* is/are rejected.

7)☒ Claim(s) *32-34,43-47 and 49-53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 05/22/2006 elected with traverse Group 12 (claims 32-34, 38 and 43-53) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 05/22/2006 elected with traverse Group 12 (claims 32-34, 38 and 43-53) drawn to an isolated mutant phytase having modification of amino acid residue 228 of SEQ ID NO:2, for examination. Groups 1-11 and 13-56 (claims 1-31, 35-37, 39-42 and 54-92) of election/restriction-office action of date 03/25/2006 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Applicants arguments that there would be no undue burden on the examiner to examine all claims directed mutant phytase is found not persuasive because while the search for each of these distinct groups would be overlapping it would not be coextensive. Art that applies for one mutant phytase may or may not be relevant to the others. Therefore the restriction is maintained and made FINAL.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 09/13/2002 for US provisional application 60/410736.

Objections

Claims 32-34, 43-47 and 49-53 are objected to as reciting non-elected subject matter.

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, 2nd paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the inventions.

Claim 33 is not further limiting of claim 33. Furthermore; the term "pure or non-pure" in claim 33 is a relative term which renders the claim indefinite. How pure or how non-pure it is? The term "pure or non-pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-34, 38 and 43-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the inventions.

These claims are directed to a genus of modified phytase or foodstuff containing the said phytase has at least one mutation (i.e., substitution of a residue equivalent 50, 91, 94, 228, 262, 300 and 301 of SEQ ID NO: 2) and has 96% sequence identity to any 100 amino acid portion of SEQ ID NO: 2. The specification teaches the structure of only a few representative species of such variants each with only a small number of altered amino acids compared to the parent phytase. A sufficient description of a genus may be achieved by recitation of a representative number of species defined by complete structure or a

recitation of structural features common to members of the genus which features constitute a substantial portion of the genus. The recited structural feature of the genus (i.e.,at least one mutation (i.e., substitution of a residue equivalent 50, 91, 94, 228, 262, 300 and 301) of SEQ ID NO: 2 and has 96% sequence identity to any 100 amino acid portion of SEQ ID NO: 2.) does not constitute a substantial portion of the genus as any 100 amino acids is insufficient for phytase activity, the remainder of the structure of any polypeptide having phytase activity is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 32-34, 38 and 43-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified phytase or food stuff wherein said variant has phytase activity and at least 95% homology to SEQ ID NO: 2, and comprises of one or more mutations selected

from the group consisting of substitution of the residue equivalent to 50, 91, 94, 228, 262, 300 and 301 of SEQ ID NO:2).does not reasonably provide enablement for any variant having only 96% sequence identity to any 100 amino acid residue portion of SEQ ID NO: 2 comprising one or more mutations selected from the group consisting of substitution of the residue equivalent to 50, 91, 94, 228, 262, 300 and 301 of SEQ ID NO:2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 32-34, 38 and 43-53 are so broad as to encompass any phytase which has 96% sequence identity to any 100 amino acids fragments of SEQ ID NO: 2 and comprising one or more mutations selected from the group consisting of a substitution of the residue corresponding to 50, 91, 94, 228, 262, 300 and 301 of SEQ ID NO:2. Thus, the currently claimed genus includes many variants with an enormous number of alterations of the parent enzyme. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of modified phytases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in

which the proteins' structure relates to its function. However, in this case the disclosure is limited to only a few representative species of such modified phytase each with only a small number of altered amino acids compared to the parent phytase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any phytase because the specification does **not** establish: (A) regions of the protein structure which may be multiply modified without effecting phytase activity; (B) a rational and predictable scheme for major modifications to any phytase at large numbers of residues with an expectation of obtaining the desired biological function; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number

of amino acid modifications of any modified phytase which has 96% sequence identity to any 100 amino acids fragments of SEQ ID NO: 2 and wherein said variant comprises one or more mutations of the residue corresponding to residue of 50, 91, 94, 228, 262, 300 and 301 of SEQ ID NO:2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of α-amylases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-34, 43, 45 and 47 and 49-53 rejected under 35 U.S.C. 103(a) by Bartok et al (US 6599735) in view of Stafford et al. (US Pat 6,475,762 which claim priority to US 60/148,960 8/13/1999).

Burtok et al. (US Pat 6599735), teach the use mutant phytase from *Aspergilluss niger* wherein amino acid residues in substrate binding region, Q50, K91, K94 are mutated for better thermo stability, lower pH enzyme activity.

Stafford et al. teach the phytase of SEQ ID NO: 3 from Aspergilluss niger having amino acid sequence which has 100% sequence identity to the SEQ ID NO: 2 of the instant application and also teach the said pytase as animal feed composition.

Since mutation of amino acid residues in substrate binding region, especially Q50, K91, K94, of *Aspergillus niger* phytase (as taught by Burtok et al) gave better thermo stability, lower pH enzyme activity; similar types of mutation of phytase of SEQ ID NO: 3 (taught by Stafford) from also *Aspergillus niger,* which is structurally homologous to the phytase of Burtok, would have been also expected to give better thermo stability, lower pH enzyme activity because a skilled artisan would have reasonably expected both phytase to be highly similar in 3-dimensional structure such that similar mutation would expected to have similar effects. Claims 51-53 further contain additional ingredients such as soybean meal , vitamin, antibiotics in addition to mutant phytase. As these are well known animal feed ingradiants and Stafford et al. teach use of phytase in animal feeds, it would have been obvius to one of ordinary skill in the art to add these ingredients to major constituent (in this case mutant phytase) to make food stuff.

As such it would have been obvious to one of ordinary skill in the art to use *Aspergilluss niger* pytase of SEQ ID NO: 3 of Stafford et al. and mutate residues Q50, K91, K94 for better thermo stability and lower pH enzyme activity as taught by Burtok et al which can be also animal foodstuff.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner, Art Unit 1652

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